Bioprinting of dual ECM scaffolds encapsulating limbal stem/progenitor cells in active and quiescent statuses.

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Public Summary:
Limbal stem cell deficiency and corneal disorders are among the top global threats for human vision. We have developed a new bioprinting method for the corneal stem cells for corneal reconstruction.

Scientific Abstract:
Limbal stem cell deficiency and corneal disorders are among the top global threats for human vision. Emerging therapies that integrate stem cell transplantation with engineered hydrogel scaffolds for biological and mechanical support are becoming a rising trend in the field. However, methods for high-throughput fabrication of hydrogel scaffolds, as well as knowledge of the interaction between limbal stem/progenitor cells (LSCs) and the surrounding extracellular matrix (ECM) are still much needed. Here, we employed digital light processing (DLP)-based bioprinting to fabricate hydrogel scaffolds encapsulating primary LSCs and studied the ECM-dependent LSC phenotypes. The DLP-based bioprinting with gelatin methacrylate (GelMA) or hyaluronic acid glycidyl methacrylate (HAGM) generated microscale hydrogel scaffolds that could support the viability of the encapsulated primary rabbit LSCs (rbLSCs) in culture. Immunocytochemistry and transcriptional analysis showed that the encapsulated rbLSCs remained active in GelMA-based scaffolds while exhibited quiescence in the HAGM-based scaffolds. The primary human LSCs encapsulated within bioprinted scaffolds showed consistent ECM-dependent active/quiescent statuses. Based on these results, we have developed a novel bioprinted dual ECM 'Yin-Yang' model encapsulating LSCs to support both active and quiescent statues. Our findings provide valuable insights towards stem cell therapies and regenerative medicine for corneal reconstruction.